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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/259,658	02/26/99	COLYER J	04256/79245

EXAMINER	
PORTNER, V	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/259,658	Applicant(s) Colyer
	Examiner Portner	Group Art Unit 1645

☒ Responsive to communication(s) filed on *Feb 5, 2001* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-18 and 20* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-18 and 20* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim 20 has been added

Claims 1-18 and 20 are pending.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Withdrawn

2. Claims 1-4, 6,12-13, 16, 18 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 6-7, and 18 rejected under 35 U.S.C. 102(e) as being anticipated by Bronstein et al (US Pat. 5,849,495).

4. Claims 16 and 18 rejected under 35 U.S.C. 102(b) as being anticipated by Tsien et al (5,439,797).

5. Claims 1-7, 13-16 rejected under 35 U.S.C. 102(e) as being anticipated by Tsien et al (US Pat.5,981,200).

6. Claim 13 rejected under 35 U.S.C. 102(e) as being anticipated by Gallatin et al (US Pat 5,989,843 or. 5,837,822).

7. Claim 17 rejected under 35 U.S.C. 102(b) as being anticipated by Decher et al (US Pat. 5,208,111).

Rejections Maintained

8. Claims 8 and 14 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record in paper number 10, paragraph 5, subparagraphs e and h. Claim 8 still has the phrase "the species". This phrase lacks antecedent basis in claim 1 from which it depends. Claim 14, recites that the immobilized polypeptide is susceptible to "covalent modification", all polypeptides are susceptible to chemical covalent modification. How one polypeptide would be suspectable and the other not is not clearly defined.

9. Claims 1-5, 8, 12-14, 16, 18 rejected under 35 U.S.C. 102(e) as being anticipated by Bronstein (US Pat. 5,849,495), for reasons of record in paper number 10, paragraph 5.

10. Claims 1-7,14-15 rejected under 35 U.S.C. 102(b) as being anticipated by Tsien et al (5,439,797) for reasons of record in paper number 10, paragraph 6.

[redacted]

11. Claims 1-7,14 rejected under 35 U.S.C. 102(b) as being anticipated by Lakowicz et al (US Pat. 5,631,169) for reasons of record in paper number 10, paragraph 8.

12. Claims 1-6,10-14, 18 rejected under 35 U.S.C. 102(e) as being anticipated by Gallatin (US Pat 5,989,843 or. 5,837,822) for reasons of record in paper number 10, paragraph 9.

13. Claims 1 and 9 rejected under 35 U.S.C. 102(b) as being anticipated by Sehr (US Pat. 5,341,215) for reasons of record in paper number 10, paragraph 10.

14. Claim 17 rejected under 35 U.S.C. 102(e) as being anticipated by Mills (US Pat. 5,773,592) for reasons of record in paper number 10, paragraph 12.

Response to Arguments

15. The rejection of claims 1-5, 8, 12-14, 16, under 35 U.S.C. 102(e) as being anticipated by Bronstein et al (US Pat. 5,849,495) is argued that the "substrates CSPD and ATToPhos TM are not associated with a polypeptide as required by claims 2 and 3, from which claims 6 and 7 depend and the energy transfer is between the substrates, but they are not labels associated with a polypeptide as required by claim 2 or 3, they do not "assay the modification of at least one of the polypeptides by measuring the association of the second polypeptide to the first polypeptide".

The functional limitation "modification" recited in claim 1, is argued to not be met by the disclosure of Bronstein. Bronstein is also asserted to not teach modulation of modification of a polypepeptide using a modifying agent as recited in claim 18.

16. Applicant's arguments filed with respect to Bronstein with respect to claim limitations recited in claims 1-3 have been fully considered but they are not persuasive because claim limitations recited in claims 2 and 3 define the polypeptides as being associated with a label. The two polypeptides used in the Hybritech Prostate Specific Antigen(PSA) assay are both associated with a label, specifically one is conjugated, covalently labeled with alkaline phosphatase and the other a bead. One of the polypeptides was contacted with an agent that was capable of covalently modifying the polypeptide to include a detectable label prior to assaying the modification of the association of the two polypeptides upon binding of the analyte in the test sample.

17. Applicant's arguments filed with respect to the definition and the assaying of *modification* have been fully considered but they are not persuasive because the definition of modification set forth in the instant specification and quoted on page 8 of the Amendment dated February 5, 2001, states that the term "modification" "may also include binding of one or more molecules of test sample to a polypeptide." Clearly the assay that measures the presence of PSA in a test sample through binding of first and second polypeptides associated with one or more PSA molecules. The presence of this binding is assayed through presence and amount of fluorescence energy transfer produced in the sample through the production of a detectable signal resulting from enzymatic activity

associated with one of the two polypeptides. The disclosure of Bronstein meets the claim limitations of claim 1 based upon the definition provided in the instant specification.

18. The rejection of claims 1-7,14-15 under 35 U.S.C. 102(b) as being anticipated by Tsien et al (5,439,797) is argued by asserting that claim 1 requires "covalent modification of at least one of the polypeptides" which results in modulation of the association of the polypeptides of the association, and exemplifies enzymatic modification as an example of covalent modification.

19. Applicant's arguments filed with respect to Tsien have been fully considered but they are not persuasive because Tsien does disclose that through binding of an analyte in the sample, a modification of the binding between the first and second polypeptides results in a modification of the association of the two polypeptides that is assayed through a change in excitation wavelength (col.4, lines 1-13 and col. 7, lines 32-38).

The claim limitation "covalent modification" is recited in the "providing step", a step prior to the polypeptides being contacted with each other. No covalent interactions are required in claim 1. The covalent modification argued is not commensurate in scope with the now claimed invention that does not require that a covalent modification take place; the claim limitation defines a conditional relationship if a covalent modification is introduced to one of the two polypeptides.

20. The rejection of claims 1-7,14 under 35 U.S.C. 102(b) as being anticipated by Lakowicz et al (US Pat. 5,631,169) is argued to not teach "a polypeptide pair comprising first polypeptide and a second polypeptide capable of associating, wherein the association of the polypeptides is detectable, and covalent modification of at least one of the polypeptides results in modulation of the association."

21. Applicant's arguments filed with respect to Lakowicz have been fully considered but they are not persuasive. The claim limitation "covalent modification" is recited in the "providing step", a step prior to the polypeptides being contacted with each other. No covalent interactions are required in claim 1.

The covalent modification argued is not commensurate in scope with the now claimed invention that does not require that a covalent modification to take place; the claim limitation defines a conditional relationship if a covalent modification is introduced to one of the two polypeptides.

Applicant's arguments do not comply with 37 CFR 1.111© because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. Further, they do not show how the amendments avoid such references or objections.

22. The rejection of claims 1-6,10-12, 14, 18 under 35 U.S.C. 102(e) as being anticipated by Gallatin et al (US Pat 5,989,843 or. 5,837,822) is argued to not teach "a polypeptide pair comprising first polypeptide and a second polypeptide capable of associating, wherein the

association of the polypeptides is detectable, and covalent modification of at least one of the polypeptides results in modulation of the association."

23. Applicant's arguments filed with respect to Gallatin et al have been fully considered but they are not persuasive. The claim limitation "covalent modification" is recited in the "providing step", a step prior to the polypeptides being contacted with each other. No covalent interactions are required in claim 1.

The covalent modification argued is not commensurate in scope with the now claimed invention that does not require that a covalent modification take place. A component of the sample is not defined to function to covalently modify either one or both of the first or second polypeptides. The claim limitation defines a conditional relationship if a covalent modification is introduced to one of the two polypeptides. Applicant's arguments are not commensurate in scope with the claimed invention.

24. The rejection of claims 1 and 9 rejected under 35 U.S.C. 102(b) as being anticipated by Sehr (US Pat. 5,341,215) is argued to not teach "a polypeptide pair comprising first polypeptide and a second polypeptide capable of associating, wherein the association of the polypeptides is detectable, and covalent modification of at least one of the polypeptides results in modulation of the association."

25. Applicant's arguments filed with respect to Sehr have been fully considered but they are not persuasive. The claim limitation "covalent modification" is recited in the

"providing step", a step prior to the polypeptides being contacted with each other. No covalent interactions are required in claim 1.

The covalent modification argued is not commensurate in scope with the now claimed invention that does not require that a covalent modification take place. A component of the sample is not defined to function to covalently modify either one or both of the first or second polypeptides. The claim limitation defines a conditional relationship if a covalent modification is introduced to one of the two polypeptides. Applicant's arguments are not commensurate in scope with the claimed invention.

26. The rejection of claim 17 under 35 U.S.C. 102(e) as being anticipated by Mills (US Pat. 5,773,592) is stated that the claimed invention is drawn to a composition of "a polypeptide pair comprising a first polypeptide immobilized to a support and a second polypeptide bound to the first polypeptide" and asserts that "the second polypeptide of Mills is not bound to the first polypeptide.

27. Applicant's arguments filed with respect to Mills have been fully considered but they are not persuasive. Contrary to Applicants assertion, the first and second polypeptides of Mills are bound to each other through a biocompatible polymer. Applicant argues specific binding partner type interaction as being required by the claim. While this type of binding is clearly within the scope of the claims, the claimed invention recited in claim 17, is not limited to specific binding partners, but only requires the presence of two polypeptides bound to each other. The type of binding recited in claim

17, is not defined to be specific binding partner binding but may be any type of binding, to include covalent bounds introduced between two polypeptides.

The claimed invention defines a polypeptide pair that is:

immobilized

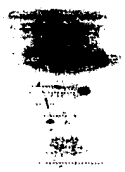
binding of the polypeptide pair must be detectable

polypeptide modification results in modulation of the binding.

The two polypeptides of Mills function as a polypeptide pair that are bound to each other through a biocompatible polymer and are immobilized. Assaying of the polypeptide pair is detectable through the interactions of the polypeptides, and the luminide molecules. The modification of the glucose oxidase through binding of glucose, causes modulation of the binding of the insulin to the glucose oxidase through the release of the insulin from the polypeptide pair.

The reference teaches: "[T]he immobilized enzyme reacts with glucose at a rate proportional to the ambient glucose concentration to produce peroxide which reacts with the functionality molecules of the attached luminide molecules to effect release of insulin. Because the insulin release is in proportion to the glucose concentration this macromolecular agent represents . very effective diabetic therapy and results in the modulation of binding between the polypeptide pair. Mills discloses all of the elements recited in the claim, and therefore anticipates the claimed invention.

New Claim Limitations/New Grounds of Rejection



Claim Rejections - 35 U.S.C. § 112

28. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

29. Claim 1 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 has been amended to recite the phrase "d) contacting said immobilized polypeptide or said binding partner polypeptide with said sample;", which step follows step c) which recites "contacting the immobilized polypeptide with the second polypeptide", wherein the polypeptides are define to be capable of associating with each other (section a) of the claim). It is not clear how the immobilized polypeptide **or** the binding partner polypeptide can be contacted with a sample when both polypeptides have already been contacted with each other. How can the sample be contacted with only one of the polypeptides when both polypeptides are co-located with each other as set forth in step c) of the claim. The recitation of the word "or" in section d) does not distinctly claim Applicant's invention. Clarification of what actually is being carried out so only one or the other polypeptides will be contacted with the sample is requested.

Claim 1 has been amended to recite the phrase " wherein the association of the polypeptides is detectable, and covalent modification of at least one of the polypeptides results in modulation of the association." A "wherein" clause can provide clarity to a claim, but does not

define positive recitation methods step. Claim 1 does not recite the covalent modification of any of the polypeptides, but defines a potential relationship between the polypeptides if one or both of them, at some future time, are covalently modified.

Claim 20 has been added that further clarifies a potential relationship by reciting "wherein said covalent modification is an enzymatic modification". How claim 20 further limits the method of claim 1 is not clearly pointed out because an enzymatic agent that would function to covalently modify any of the polypeptides of claim 1 has not been provided. No other agents have been used or added to the method of claim 1 that would covalently react with either of the polypeptides. If Applicant intends for a covalent modification to take place it should be recited in claim 1 through addition of method steps that positively recite covalent action by an agent. Upon clarification of claim 1 to comprise the use of an agent that causes covalent modification of the polypeptides, claim 20 would be further limiting of claim 1. Clarification is requested.

Claim Rejections - 35 U.S.C. § 102

30. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Please Note: The following art rejections over claims 1 and 20 are being made of record, in light of the claims being read to require covalent modification induced by enzymatic activity as recited in newly submitted claim 20 which depends from independent claim 1. The examiner is reading the word to be a type of polypeptide.

31. Claims 1 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Avruch et al (US Pat. 5,582,995).

The claimed invention is drawn to a method of analyzing a sample through providing a binding pair of polypeptides, one of which is immobilized. The polypeptides are contacted with a sample and enzyme (claim 20) modification of at least one of the polypeptides is assayed.

Avruch et al disclose a method of assaying a sample which comprises:

providing two polypeptides that are capable of associating (enzyme and protein substrate; claim 1, 7-9)

immobilizing the first polypeptide (polypeptide substrate, claim 19)

contacting the immobilized polypeptide and the second polypeptide with the sample (test substance, claim 1); and

assaying any enzyme modification of one or both of the polypeptide (claim 1, section (b).

In summary, Avruch disclose a method of assaying a sample that utilizes the following components.

The two polypeptides are a protein substrate containing a CAAX motif, (see claims 1,7) and farnesyl-protein transferase. (see claim 1)

The protein substrate is immobilized prior to contact with the sample (claim 19) and is susceptible to covalent modification (covalent farnesyl residue incorporation into the substrate polypeptide, see claims 7-9).

The sample of Avruch is a test substance. (claim 1) .

The reference anticipates the now claimed invention.

32. Claims 1 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Josiah et al (6,146,842)

The claimed invention is drawn to a method of analyzing a sample through providing a binding pair of polypeptides, one of which is immobilized. The polypeptides are contacted with a sample and enzyme (Instant invention, claim 20) modification of at least one of the polypeptides is assayed.

Josiah et al disclose a method of assaying a sample which comprises:

providing two polypeptides that are capable of associating (enzyme and protein substrate; claim 12 and 15)

immobilizing the first polypeptide (polypeptide substrate, claim 19)

contacting the immobilized polypeptide and the second polypeptide with the sample (test compound, claim 12); and

assaying any enzyme modification of one or both of the polypeptide (claim 12 and 15, section (b).

In summary, Josiah disclose a method of assaying a sample that utilizes the following components.

The two polypeptides are a protein substrate, (see claim 12)

and farnesyl or geranylgeranyl transferase. (see claim 13)

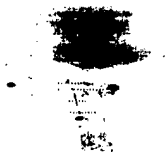
The protein substrate is immobilized prior to contact with the sample (claim 19) and is susceptible to covalent modification (see claim 14).

The sample of Josiah is a test compound. (claim 12) .

The reference anticipates the now claimed invention.

Conclusion

33. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP



§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

34.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
April 11, 2001

L. F. Smith

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